Behavioral-Based Deferrals in the NAT Era: Design and Efficiency of Current FDA Recommendations

Alan E. Williams, Ph.D.
Director, Division of Blood Applications
Office of Blood Research and Review
CBER, FDA

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Importance of Accurate Donor Qualification

- Maximize Blood Safety
  - Known agents with laboratory screen
    (window period, testing errors, release errors, staff protection)
- Known or unknown agents for which there is no laboratory screen
  - Donor screening may be sole protection
  - Threat may be recognized and partially characterized (vCJD)
  - Threat may be unrecognized, but ineligibility for individuals with behaviors that heighten exposure to parenteral agents may be prudent (there is a high probability that other parenteral agents remain to be discovered.)
- Minimize Donor Loss
- Minimize Negative Operational Impact
  - e.g. Post-donation information
- Minimize Staff Exposure to Infectious Donations

Stages of Donor Qualification

- Exclusion of risk populations
  - Paid donors (via labeling), prisoners
- **Self deferral prior to appearance for donation**
  - **(educational materials, conversation with staff)**
- Self-deferral at collection site prior to interview
  - (on-site educational materials)
- Deferral by staff during interview
  (with or without self-administered questionnaire)
- Post-Donation Information
  - (donor call-back, third party information, subsequent donation history)

Five Principles for FDA Donor Eligibility Considerations

I. Ensure consistency and risk/benefit balance, including determination/modeling of sensitivity, specificity, predictive value when possible.

"Safety" is context – dependent, and includes continued availability of medically-necessary products

II. Strive for science-driven policy, but recognize need to act in the interest of public health when scientific answers not fully available (prudent measures)

Six Principles for FDA Donor Eligibility Considerations (cont.)

**III. Ensure that any changes in existing policy result in improved or equivalent safety

Six Principles for FDA Donor Eligibility Considerations (cont.)

IV. Discuss proposed policy within FDA, HHS; provide opportunities for industry/public comment.

V. Provide liaison support to organized industry efforts to define voluntary standards

Selected FDA- Recommended Blood Donor Behavioral Deferrals
(As included in the current DHQ)

- In the past 12 months….
  - **Had sexual contact with anyone who has HIV/AIDS or has had a positive test for the HIV/AIDS virus?**
  - **Had sexual contact with a prostitute or anyone else who takes money or drugs or payment for sex?**
  - **Had sexual contact with anyone who ever used needles to take drugs ((or steroids)), or anything not prescribed by their doctor?**

Revised Recommendations for the Prevention of Human Immunodeficiency Virus (HIV) Transmission in Blood and Blood Products – 4/23/92

Selected FDA- Recommended Blood Donor Behavioral Deferrals (cont.)
(As included in the current DHQ)

- In the past 12 months….
  - **Had sexual contact with anyone who has hemophilia or has used clotting factor concentrates?**
  - **Females - Had sexual contact with a male who has ever had sexual contact with another male?**

Revised Recommendations for the Prevention of Human Immunodeficiency Virus (HIV) Transmission in Blood and Blood Products – 4/23/92

Selected FDA- Recommended Blood Donor Behavioral Deferrals (cont.)
(As included in the current DHQ)

- Since 1977… (AIDS case recognition in US)
  - **From 1977 to the present, have you - Received money, drugs, or other payment for sex?**
  - **– From 1977 to the present, have you – Males – had sexual contact with another male even once?**

Revised Recommendations for the Prevention of Human Immunodeficiency Virus (HIV) Transmission in Blood and Blood Products – 4/23/92

Selected FDA- Recommended Blood Donor Behavioral Deferrals (cont.)
(As included in the current DHQ)

- Ever…
  - **Used needles to take drugs, ((steroids)), or anything <u>not</u> prescribed by your doctor?** (amplified exposure to known and unknown parenteral agents)

Revised Recommendations for the Prevention of Human Immunodeficiency Virus (HIV) Transmission in Blood and Blood Products – 4/23/92

  - **Had sexual contact with anyone who was born in or lived in Africa?** (potential long-term asymptomatic infection with group O HIV)

Interim Recommendations for Deferral of Donors at Increased Risk for HIV-1 Group O Infections – 12/11/96

Assessing the Efficacy of Donor Deferrals

Sources of Data

Donors

1. Marker prevalence and incidence
2. Rates of deferral, PDI, other operational measures
3. Post-donation risk survey (marker positive donors)
4. Post-donation risk survey (all donors)

General population

1. Marker prevalence
2. ((Limited behavioral risk surveys))
3. FT donor ~ Untested general population after one time of donor eligibility screening

** Comparisons may not be rigorous, but make use of only available data ***

Examples: Reduction of infectious disease marker prevalence/(incidence) in accepted blood donors

1) … compared with general population

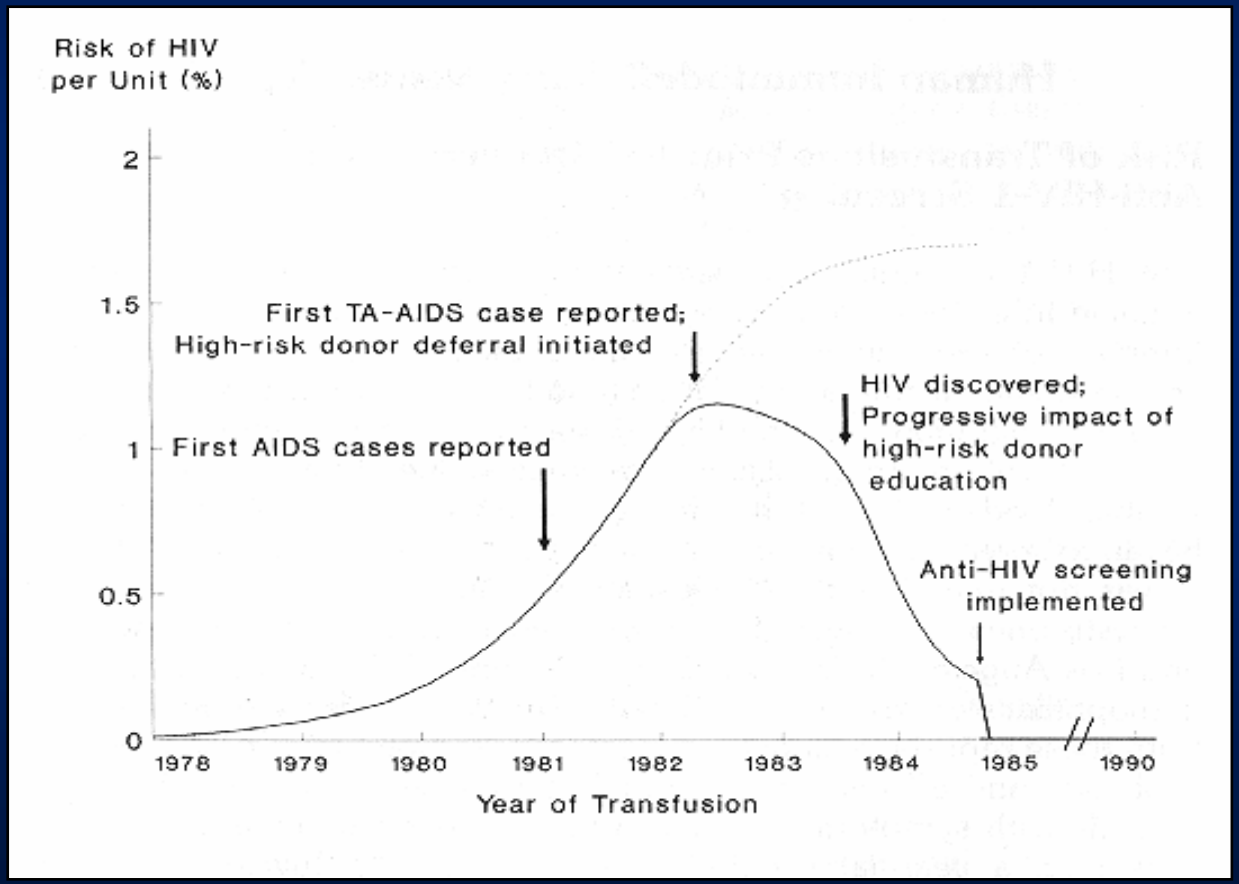
0.47% confirmed HIV+ in donor-age general population (McQuillan, 1994)

0.03% confirmed HIV+ in FT Donors (REDS survey circa 1995)

➡ **93.6%** reduction in HIV seroprevalence

2) … over time

Approximately 90% Reduction of PT HIV-1 Transmission in San Francisco Due to Donor Screening Prior to anti-HIV Screening (MP Busch 1992)



Reduction of infectious disease risk in accepted blood donors

1) … compared with general population

4.1% prevalence of MSM - past 5 yrs in male general population (Laumann 1994)

0.57% MSM-77 risk in accepted male donors

(Williams 1997)

➡ 86.1% reduction

Reduction of infectious disease risk in accepted blood donors

2) … compared with general population

3.9% IDU since 1978 in general population ((Dallas Household Survey 1994)

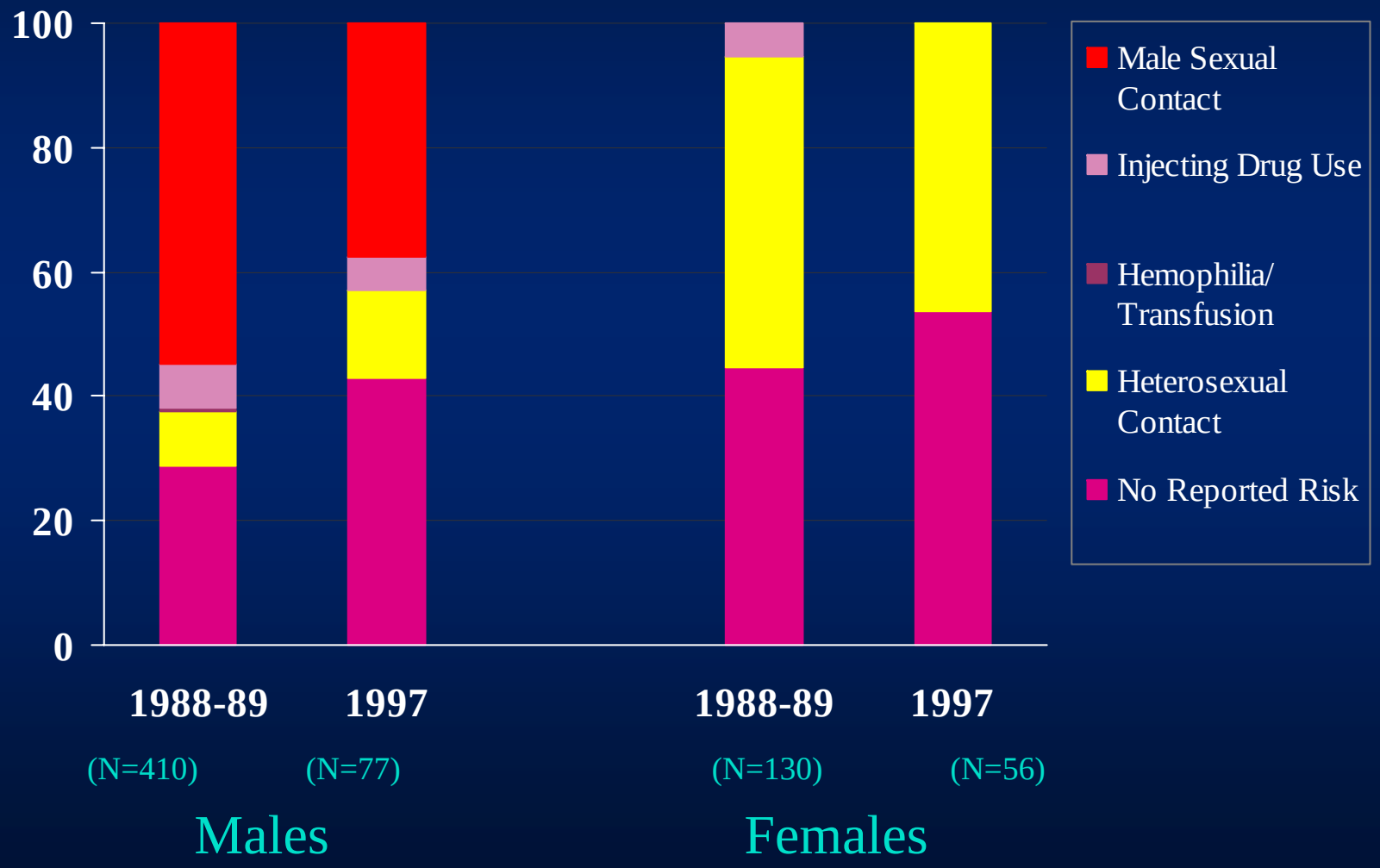
0.51% IDU-ever among accepted donors (Williams 1997)

➡ 86.9% reduction

Observations about False Negative Behavioral Screening of Donors

- Interviews of accepted, seropositive donors frequently identify behavioral risks that should have prevented donation.
  - These studies are important to monitor the risk exposures that resulted in infection and rule out unusual modes of infection transmission.

HIV Seropositive Donors by Exposure Category



Observations about False Negative Behavioral Screening of Donors

- Surveys of accepted, unselected donors also identify behavioral risks that should have prevented donation. These studies define the behavioral risk burden in the donor pool that contributes to incident infection.

REDS Study: Measurement of Deferrable Risk JAMA 1997;277:967-72

- In past year
  - Prostitute use (males) [0.5%]
  - Female sex with MSM [0.3%]
  - Syphilis/gonorrhea [0.1%]
  - Sex with IDU [0.4%]
  - Needle stick [0.3%]
  - Transfusion [0.03%]
- Since 1977
  - MSM [0.6%]
- Ever
  - IDU [0.5%]
- 1.9% of donors reported one or more risks
- ~ 241,800 U.S. donors/yr.

REDS Study: Correlations with MSM Deferrable Risk Transfusion 2005;45:404-413

- 280/25,168 male respondents reported MSM since 1977 (1.2%)
  - cf: 0.6% in similar 1993 survey
  - Reactive screening tests correlated with MSM < 5 yrs, but not > 5 yrs
  - Other deferrable risks (IDU; money or drugs for sex) and self-reported HIV test-seeking higher in <u>all</u> subgroups reporting MSM since 1977 cf. non-MSM males.

HIV risk in donors reporting MSM in the past year

- From the 1998 REDS survey, 92/25,168 male respondents reported MSM in the past year (0.36%).This subgroup of male donors was also higher for all other TTVI risks, HIV test-seeking, test markers, and lifetime sex partners.
- HIV window period << one year.
- Approximately 16,000 donors (MSM< 1 year) are a major source of incident HIV entering the blood supply.
- Improved behavioral science to identify and interdict blood donation by overtly high risk donors remains a priority.

Behavioral Science Perspective

- Information about personal behaviors is inherently difficult to collect.
  - Social acceptability of information
  - Response rates are low/missing data and inconsistencies are frequent
    (regulated blood establishments are special case)
  - People tend to avoid careful reading
  - Improvement in quality with serial data collections (all qualified plasma donors and most WB most donors are repeat)

- Donor forms own basis for risk assessment
  - Denial
  - Lack of respect for policy

- External factors prevent correct self-deferral
  - Secondary gain from donation
  - Peer pressure and Environment
  - Comprehension
  - Question complexity

Applied Research

- Uniform Donor History Task Force
  - Multi-institutional - FDA encouragement and participation
  - Goal: “Streamline” the current AABB UDHQ Question via review of content, wording, relevance
  - Format (Consider “capture” /“interval” Questions)
    - Computerized donor interface
    - Improved pre-donation education.
  - Validation of key questions - structure, content, comprehension (ARC, NCHS)

Current Research (Methodology)

- Audio-CASI (Turner, et al)
  - fully private
  - literacy not required
  - fully standardized - no interviewer variability
  - multi-lingual option
  - visual aids
  - respondent “in-control”

Conclusions:

- FDA considerations of donor deferral are grounded on several well-defined paradigms that are science-based, but also consider the context of risk, and the inevitable scientific uncertainties.
- Based upon limited data from analogous donor screening situations, we estimate an 85 - 99% sensitivity of current blood donor screening procedures.
- Further behavioral research in this area is critical; particularly methods that will support the identification and interdiction from donation of overtly high risk donors who fail to self-defer.